Remarks

The final Office Action dated December 21, 2007 has been reviewed, and the above-mentioned amendments and following remarks are made in response thereto. In view of the following remarks, Applicants respectfully request reconsideration of this application and timely allowance of the pending claims. Claims 1, 4-8, 10-39, 41-72, 74-79, 81-82, 84-86, 88-95, 104-105, 107-110, 128-129, 131-132, 134-140, 142, 152, 154-157 and 174-272 are pending and claim 1 is amended. Claims 9, 73, 80, 83, 87, 96-103, 106, 111-127, 130, 133, 141, 143,-151, 153, 158-173 are cancelled without prejudice or disclaimer to the subject matter claimed therein. Written support for the claim amendments are found throughout the specification and in the original claims, thus Applicants submit that no prohibited new matter has been added.

Rejections under 35 U.S.C. 102(b)

Claims 1, 4 ,6, 8, 36, 37, 41-45, 50-51, 53, 72, 80, 96-100, 106, 111, 112, 113, 127, 133, 141, 143-145, 147, 153 and 158-160 were rejected under 35 U.S.C. 102(b) as being anticipated by Levine (U.S. Patent Application Publication No. 2002/0016331) ("*Levine*"). In particular, the Examiner alleged that *Levine* teaches a method of treating pain, including neuropathic pain, comprising administering to a human a composition comprising an opioid antagonist (Office Action at page 5). Applicants respectfully traverse.

Anticipation is established when a single prior art reference expressly or inherently discloses, each and every element of a claimed invention. *EMI Group North America v. Cypress Semiconductor*, 268 F.3d 1342, 1350 (Fed. Cir. 2001); *Telemac Cellular Corp. v. Topp Telecom Inc.*, 247 F.3d 1316, 1327 (Fed. Cir. 2001). There must be no difference between the claimed invention and the reference disclosure as viewed by one of ordinary skill in the art. *Scripps Clinic & Research Foundation v. Genentech*, 927 F.2d 1565, 1576 (Fed. Cir. 1991).

Without acquiescing to the merits of the Examiner's rejection, and solely to further the prosecution of the pending application, Applicants have rewritten claim 1 to include the limitations of claim 73. Notably, claim 73 was not rejected by the Examiner under 35 U.S.C. 102(b) as being anticipated by *Levine*. Further, claims 9, 73, 80, 83, 87, 96-103, 106, 111-127, 130, 133, 141, 143,-151, 153, 158-173 are cancelled by way of this Amendment, thereby rendering any rejections as to these claims moot.

With regard to the rejection of the pending claims, Applicants have amended claim 1 to recite that the amount of opioid antagonist is from about 0.000001 mg to less than about 1.0 mg, the amount of opioid agonist is from about 0.1 mg to about 300 mg, the opioid antagonist is naltrexone, nalmefene or naloxone and that the opioid agonist is morphine, oxycodone, oxymorphone, hydrocodone or tramadol. Given that none of these limitations are neither disclosed nor inherent from *Levine*, *Levine* fails to disclose each and every element of the claimed invention. Accordingly, Applicants respectfully request that the rejection of claims 1, 4, 6, 8, 36, 37, 41-45, 50-51, 53, 72, 80, 96-100, 106, 111, 112, 113, 127, 133, 141, 143-145, 147, 153 and 158-160 under 35 U.S.C. 102(b) as being anticipated by *Levine* be reconsidered and withdrawn.

Additionally, claims 1, 4, 6, 8-10, 14, 36-38, 41 ,42, 44 ,45, 47, 48, 49, 50, 80, 87, 96, 97, 99, 100, 102, 103, 106, 113, 115, 119, 120, 121, 122, 123, 127, 133, 141, 143, 144, 146, 147, 149, 150, 151, 153, 160, 162, 166, 167, 168, 169 and 170 were rejected under 35 U.S.C. 102(b) as being anticipated by Crain et al. (US Patent 5,580,876) ("*Crain*"). Specifically, the Examiner purported that *Crain* teaches a method of administering an analgesic or sub-analgesic amount of a bimodially-acting opioid receptor agonist and an amount of an excitatory opioid receptor antagonist formulated in compositions with a pharmaceutically acceptable carrier. Applicants respectfully traverse the rejection.

Without acquiescing to the merits of the Examiner's rejection, and solely to further the prosecution of the pending application, Applicants have amended claim 1 to include the limitations of claim 73. Notably, claim 73 was not rejected by the Examiner under 35 U.S.C. 102(b) as being anticipated by *Crain*. Further, claims 9, 73, 80, 83, 87, 96-103, 106, 111-127, 130, 133, 141, 143,-151, 153, 158-173 are cancelled by way of this Amendment, thereby rendering any rejections as to these claims moot.

With regard to the rejection of the pending claims, Applicants have rewritten claim 1 to recite that the amount of opioid antagonist is from about 0.000001 mg to less than about 1.0 mg, the amount of opioid agonist is from about 0.1 mg to about 300 mg, the opioid antagonist is naltrexone, nalmefene or naloxone and that the opioid agonist is morphine, oxycodone, oxymorphone, hydrocodone or tramadol. Given that none of these limitations are neither

disclosed nor inherent from *Crain*, *Crain* fails to describe each and every element of the claimed invention. Accordingly, Applicants respectfully request that the rejection of claims 1, 4, 6, 8-10, 14, 36-38, 41 ,42, 44 ,45, 47, 48, 49, 50, 80, 87, 96, 97, 99, 100, 102, 103, 106, 113, 115, 119, 120, 121, 122, 123, 127, 133, 141, 143, 144, 146, 147, 149, 150, 151, 153, 160, 162, 166, 167, 168, 169 and 170 under 35 U.S.C. 102(b) as being anticipated by *Crain* be reconsidered and withdrawn.

Rejections under 35 U.S.C. 103(a)

Claims 1-4[1], 6, 8-10, 14, 22-45, 47-54, 72-74, 77, 80, 83, 87, 96-100, 102-103, 106, 111-127, 130, 133, 141, 143-147, 149-151, 153 and 158-173 were rejected under 35 U.S.C. 103(a) as being unpatentable over Mitch *et al.* (US Patent No. 5,998,434) ("*Mitch*") in view of Romans *et al.* (US Patent No. 7,015,371) ("*Romans*") and Sawynok *et al.* (US Patent No. 6,211,171) ("*Sawynok*") and Frome (US Patent Application Publication No. 2003/0060463) ("*Frome*") and Fairbanks *et al.* (US Patent No. 6,054,461) ("*Fairbanks*") and Rueter *et al.* (US Patent Application Publication No. 2003/0216448) ("*Rueter*") and Mayer *et al.* (US Patent No. 5,502,058) ("*Mayer*"). Applicants respectfully traverse the rejection.

Under 35 U.S.C. § 103, the factual inquiry into obviousness requires a determination of: (1) the scope and content of the prior art; (2) the differences between the claimed subject matter and the prior art; (3) the level of ordinary skill in the art; and (4) secondary consideration (e.g., the problem solved). *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18, 148 USPQ2d 459, 467 (1966). "[A]nalysis [of whether the subject matter of a claim is obvious] need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR Int'l Co. Teleflex, Inc.*, 127 S. Ct. 1727, 1741, 82 USPQ2d 1385, 1396 (2007) *quoting In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006); *see also DyStar Textilfarben GmBH & Co. Deutschland KG v. C.H. Patrick Co.*, 464 F.3d 1356, 1361, 80 USPQ2d 1641, 1645 (Fed. Cir. 2006) ("The motivation need not be found in the references sought to be combined, but may be found in any number of sources, including common

[1] Applicants note that the Examiner has erroneously included claims 2-3 in this rejection under 35 U.S.C., when in fact these claims were cancelled in the Response mailed on October 10, 2007.

knowledge, the prior art as a whole, or the nature of the problem itself."). The analysis supporting obviousness, however, should be made explicit and should "identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements" in the manner claimed. *KSR*, 127 S. Ct. at 1732, 82 USPQ2d at 1389.

With respect to any rejection of claims 9, 73, 80, 83, 87, 96-103, 106, 111-127, 130, 133, 141, 143,-151, 153, 158-173, these claims are cancelled by way of this Amendment thereby rendering any rejections as to these claims moot.

With respect to the rejection of the pending claims, Applicants respectfully submit that *Mitch* does not enable compositions comprising an opioid antagonist in an amount from about 0.000001 mg to less than about 1.0 mg to enhance the pain-alleviating potency of an opioid agonist. The portion of *Mitch* relied upon by the Examiner merely states that the term "opioid" used throughout the application may refer to opioid agonist-antagonists. Nowhere in the application is the amount of antagonist that is effective to enhance the pain-alleviating potency of the administered agonist described. Further, the Examiner asserts that it would have been obvious to vary and/or optimize the dose of the opioid antagonist that would enhance the potency of the opioid agonist described in *Mitch*. Applicants submit that it would not be obvious to use an opioid antagonist in the amounts claimed by Applicants (*e.g.*, from about 0.000001 mg to less than about 1.0 mg) to enhance the pain alleviating affects of an opioid agonist because an antagonist in the composition would be presumed by a skilled artisan to reduce the pain alleviating affect of the agonist, not enhance it.

Moreover, the combination of *Mitch* with *Romans*, *Sawynok*, *Frome*, *Fairbanks*, *Rueter* and/or *Mayer* fails to provide or suggest the claimed invention. As described above, the Examiner is mistaken that it would have been obvious to modify/vary the dosages of opioid agonist and opioid antagonist of *Mitch* to arrive at the instant invention. There is no suggestion or motivation from any reference singly or in combination to use an opioid antagonist in the claimed range of about 0.000001 mg to less than about 1.0 mg in combination with an opioid agonist. In fact, the skilled artisan would have deemed such a low amount of antagonist futile and would never have arrived at the claimed invention. As such, there is no motivation to combine *Mitch* with the compounds described in *Romans*, *Sawynok*, *Frome*, *Fairbanks*, *Rueter* and/or *Mayer* to arrive at the presently claimed invention. Accordingly, Applicants respectfully

request that the rejection of claims 1-4, 6, 8-10, 14, 22-45, 47-54, 72-74, 77, 80, 83, 87, 96-100, 102-103, 106, 111-127, 130, 133, 141, 143-147, 149-151, 153 and 158-173 under 35 U.S.C. 103(a) be reconsidered and withdrawn.

Moreover, claims 46, 101 and 148 were rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman & Gillman's: The Pharmacological Approach to Therapeutics (Tenth edition, page 8) ("*Goodman*"). Specifically, the Examiner asserts that it would have been obvious to one having ordinary skill in the art at the time of the invention to administer the claimed composition by any known route of drug administration as taught by *Goodman*. Applicants respectfully traverse the rejection.

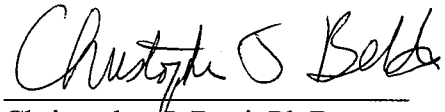
With respect to the rejection of claims 101 and 148, Applicants have cancelled these claims without prejudice or disclaimer to the subject matter claimed therein, thereby rendering the rejection as to this claim moot.

With respect to the rejection of claim 46, Applicants submit that there is no teaching, suggestion or motivation to treat neuropathic pain from *Goodman* by administering a composition comprising an opioid antagonist in an amount from about 0.000001 mg to less than about 1.0 mg or an amount of antagonist more than 40 fold less than the amount of the agonist administered to enhance the pain-alleviating potency of an opioid agonist. Applicants submit that it cannot be obvious to administer a composition that is not described in the art. Thus, it would not have been obvious to try to administer an unknown composition via the routes allegedly described by *Goodman*. Accordingly, Applicants respectfully request that the rejection of claims 46, 101 and 148 under 35 U.S.C. 103(a) be reconsidered and withdrawn.

Conclusion

Applicants respectfully submit that the present application is in condition for allowance and earnestly solicit reconsideration of same. The Examiner is respectfully requested to telephone the undersigned if he can assist in any way in expediting prosecution of this application. The Commissioner is authorized to charge any underpayment of fees or credit any overpayment of fees to Deposit Account No. 02-1818 (order no. 117789-042) for any matter in connection with this response.

Respectfully submitted,
BELL, BOYD & LLOYD LLP

BY 
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Dated: June 23, 2008